REMARKS

Claims 1-14 and 29-40 are pending in this application. Claims 1, 2, 13, 14, 29, 32, 36, 39 and 40 have been amended. It is respectfully requested that claims 41-45 be entered into this application.

In claim 1, the group $N(C(O)CF_3)$ as a definition of Z has been corrected.

The Examiner has objected to claims 2, 13, 14, and 29 and has rejected claims 1-14 and 29-40 under 35 USC 112, second paragraph. Applicants respectfully traverse these objections and rejections.

Claim 2 has been amended to correct the case of $SO_2NH(C_1\text{-}C_6$ alkyl).

Claim 13 has been amended to insert a comma between neurogenerative diseases and gastrointestinal diseases. Claim 13 has also been amended to delete "such as fibromyalgia" and "including cerebral ischemia" and to add excitotoxic neuronal damage. Support for this is found on page 26, line 7.

New claim 41 depends from claim 13 and defines the pain perception as fibromyalgia.

New claim 42 depends from claim 13 and defines the ischemic neuronal damage as cerebral ischemia.

Claim 14 has been amended to delete the phrase "such as depression and postpartum depression". New claim 43 is presented to include this subject matter. Claim 14 has been amended to delete "including a human". This is the subject matter of new claim 45.

Claim 29 has been amended to correct the subscripts in R_{24} and R_{25}.

Claim 32 has been amended to insert - - and - - between "depression" and "child".

Claim 36 has been amended to delete the word "including".

Claim 39 has been amended to depend from claim 44. Claim 44 depends from claim 14 and defines the ischemic neuronal damages as cerebral ischemia.

Claim 40 has been amended to add a period at the end of the claim.

Accordingly it is respectfully requested that the objection to the claims and the rejection of the claims be withdrawn.

It is submitted that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,

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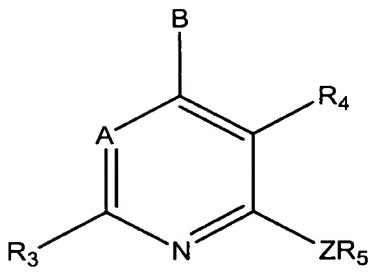
Claim 1 (Twice Amended). A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is N;

B is $-NR_1R_2$, $-CR_1R_2R_{11}$, $-C(=CR_2R_{12})R_1$, $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_2OR_1$, $-CHR_1OR_2$, $-CHR_2SR_1$,$-C(S)R_2$, $-C(O)R_2$, $-CHR_2NR_1R[2]_2$, $-CHR_1NHR_2$, $-CHR_1N(CH_3)R_2$, or $-NR_{12}NR_1R_2$;

Z is NH, O, S, -N (C_1-C_2 alkyl)-, [$-NC(O)CF_3$] $\underline{N(C(O)CF_3)}$,- or $-C(R_{13}R_{14})-$, wherein R_{13} and R_{14} are each, independently, hydrogen, trifluoromethyl or methyl, or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl, or $-C(R_{13}R_{14})$ is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R_5, which ring optionally comprises two or three further hetero members selected independently from oxygen, nitrogen, NR_{12}, and $S(O)_m$, and optionally comprises from one to three double bonds, and is optionally substituted with halo, C_1- C_4 alkyl, $-O(C_1$-C_4 alkyl), NH_2, $NHCH_3$, $N(CH_3)_2$, CF_3, or OCF_3, with the proviso that said ring does not contain any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and does not comprise more than two oxygen or $S(O)_m$ heterologous members;

R_1 is C(O)H, C(O)(C_1-C_6 hydrocarbyl), C(O)(C_1-C_6 _hydrocarbylene)(C_3-C_8 cyclohydrocarbyl), C(O)(C_3-C_8 cyclohydrocarbylene)(C_3-C_8 _cyclohydrocarbyl), C(O)(C_1-C_6 hydrocarbylene)(C_4-C_8 heterocyclohydrocarbyl), -C(O)(C_3-C_8 cyclohydrocarbylene)(C_4-C_8 heterocyclohydrocarbyl), C_1-C_6 hydrocarbyl, C_3-C_8 cyclohydrocarbyl , C_4-C_8 heterocyclohydrocarbyl, -(C_1-C_6 hydrocarbylene (C_3-C_8 cyclohydrocarbyl),C_3-C_8 cyclohydrocarbylene)(C_3-C_8 cyclohydrocarbyl), -(C_1-C_6hydrocarbylene)(C_4-C_8 heterocyclohydrocarbyl), -(C_3-C_8 cyclohydrocarbylene)(C_4-C_8 heterocyclohydrocarbyl), or -O-aryl, or -O-(C_1-C_6 hydrocarbylene)-aryl; wherein said aryl, C_4-C_8 heterocyclohydrocarbyl, C_1-C_6 hydrocarbyl, C_3-C_8 cyclohydrocarbyl , C_3-C_8 cyclohydrocarbylene, and C_1-C_6

hydrocarbylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R_8 independently selected from the group consisting of C_1-C_4 hydrocarbyl, -C_3-C_8 cyclohydrocarbyl, hydroxy, chloro, bromo, iodo, CF_3, -O-(C_1-C_6 hydrocarbyl), -O-(C_3-C_5 cyclohydrocarbyl), -O-CO-(C_1-C_4 hydrocarbyl), -O-CO-NH(C_1-C_4 hydrocarbyl), -O-CO-N(R_{24})(R_{25}), -N(R_{24})(R_{25}), -S(C_1-C_4 hydrocarbyl), -S(C_3-C_5 cyclohydrocarbyl --N(C_1-C_4 hydrocarbyl)CO(C_1-C_4 hydrocarbyl), -NHCO(C_1-C_4 hydrocarbyl), -COO(C_1-C_4 hydrocarbyl), -CONH(C_1-C_4 hydrocarbyl), -CONC$_1$-C_4 hydrocarbyl)(C_1-C_2 hydrocarbyl), CN, NO_2, -OSO_2(C_1-C_4 hydrocarbyl), S^+(C_1-C_6 hydrocarbyl)(C_1-C_2 hydrocarbyl), -SO(C_1-C_4 hydrocarbyl) and -SO_2(C_1-C_4 hydrocarbyl); and wherein the C_1-C_6 hydrocarbyl, C_1-C_6 hydrocarbylene, C_5-C_8 cyclohydrocarbyl, C_5-C_8 cyclohydrocarbylene, and C_5-C_8 heterocyclohydrocarbyl moieties of R_1 may optionally independently contain from one to three double or triple bonds; and wherein the C_1-C_4 hydrocarbyl moieties and C_1-C_6 hydrocarbyl moieties of R_8 can optionally independently be substituted with hydroxy, amino, C_1-C_4 alkyl, aryl, -CH_2-aryl, C_3-C_5 cycloalkyl, or -O-(C_1-C_4 alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally contain one or two double or triple bonds; and wherein each heterocyclohydrocarbyl group of R_1 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

R_2 is hydrogen, C_1-C_{12} hydrocarbyl, C_3-C_8 cyclohydrocarbyl , C_4-C_8 heterocyclohydrocarbyl, -(C_1-C_6 hydrocarbylene)(C_3-C_8 cyclohydrocarbyl), -(C_3-C_8 cyclohydrocarbylene)(C_3-C_8 cyclohydrocarbyl), -(C_1-C_6 hydrocarbylene)(C_4-C_8 heterocyclohydrocarbyl), -(C_3-C_6 cyclohydrocarbylene)(C_4-C_8 heterocyclohydrocarbyl), aryl, -(C_1-C_6 hydrocarbylene)aryl, or -(C_3-C_8 cyclohydrocarbylene)(aryl); wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C_1-C_6 alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C_1-C_6 alkoxy, -OH, -O-CO-(C_1-C_6 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -S (C_1-C_6 alkyl), -S(O)(C_1-C_6 alkyl), -$S(O)_2$(C_1-C_6 alkyl), S^+(C_1-C_6 alkyl)(C_1-C_2 alkyl)I', CN, and NO_2; and wherein the C_1-C_{12} hydrocarbyl, -(C_1-C_6 hydrocarbylene), and cyclohydrocarbyl gropups of 5 - 8 carbon atoms, cyclohydrocarbylene groups of 5 to 8 carbon atoms and heterocyclohydrocarbyl groiups of 5 to 8 atoms of R_2 may optionally independently contain from one to three double or triple bonds; and wherein each heterocyclohydrocarbyl group of R_2 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

or when R_1 and R_2 are as in -NHCHR_1R_2, -OCHR_1R_2, -SCHR_1R_2, -CHR_1R_2 or -NR_1R_2,

R_1 and R_2 of B may form a saturated 5- to 8-membered ring which may optionally contain one or

two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, $S(O)_m$, nitrogen or NR_{12}; and which carbocyclic ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C_1-C_4 alkyl, fluoro, chloro, bromo, iodo, CF_3, -O-(C_1-C_4 alkyl), -O-CO-(C_1-C_4 alkyl), -O-CO-NH(C_1-C_4 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_2 alkyl)(C_1-C_4 alkyl), -S(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)CO(C_1-C_4 alkyl), -NHCO(C_1-C_4 alkyl),-COO(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -CON(C_1-C_4 alkyl)(C_1-C_2 alkyl), CN, NO_2, -OSO_2(C_1-C_4 alkyl), -SO(C_1-C_4 alkyl), and -SO(C_1-C_4 alkyl), wherein one of said one to three substituents can further be selected from phenyl;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3, NH_2, NH(C_1-C_2 alkyl), $N(CH_3)_2$, -$NHCOCF_3$, -$NHCH_2CF_3$, $S(O)_m$(C_1-C_4 alkyl), $CONH_2$, -$CONHCH_3$, $CON(CH_3)_2$, -CF_3, or CH_2OCH_3;

R_4 is hydrogen, C_1-C_4 hydrocarbyl, C_3-C_5 cycloalkyl, -(C_1-C_4 hydrocarbylene)(C_3-C_5 cycloalkyl), -(C_3-C_5 cycloalkylene)(C_3-C_6 cycloalkyl), cyano, fluoro, chloro, bromo, iodo, -OR_{24} C_1-C_6 alkoxy, -O- cycloalkyl), -O-(C_1-C_4 hydrocarbylene)(C_3-C_5 cycloalkyl), -O-(C_3-C_5 cycloalkylene)(C_3-C_5 cycloalkyl), -$CH_2SC(S)O$(C_1-C_4 alkyl), CH_2OCF_3, CF_3, amino, nitro, -$NR_{24}R_{25}$, -(C_1-C_4 hydrocarbylene)-OR_{24}, -(C_1-C_4 hydrocarbylene)Cl, -(C_1-C_4 hydrocarbylene)$NR_{24}R_{25}$, -$NHCOR_{24}$, -$NHCONR_{24}R_{25}$, -CH=NOR_{24}, -$NHNR_{24}R_{25}$, -$S(O)_mR_{24}$, -$C(O)R_{24}$, -$OC(O)R_{24}$, -C(O)CN, -$C(O)NR_{24}R_{25}$, -$C(O)NHNR_{24}R_{25}$, and -$COOR_{24}$, wherein the hydrocarbyl and hydrocarbylene groups of R_4 may optionally independently contain one or two double or triple bonds and may optionally independently be substituted with one or two substituents R_{10} independently selected from hydroxy, amino, -$NHCOCH_3$, -$NHCOCH_2Cl$, -NH(C_1-C_2 alkyl), -N(C_1-C_2 alkyl)(C_1-C_2alkyl), -COO(C_1-C_4 alkyl), -COOH, -CO(C_1-C_4 alkyl), C_1-C_6 alkoxy, C_1-C_3 thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R_5 is aryl or heteroaryl and is substituted with from one to four substituents R_{27} independently selected from halo, C_1-C_{10} hydrocarbyl, -(C_1-C_4 hydrocarbylene)(C_3-C_8 cycloalkyl), -(C_1-C_4 hydrocarbylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkyl), -(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, nitro, cyano, -$NR_{24}R_{25}$, -$NR_{24}COR_{25}$, -$NR_{24}CO_2R_{26}$, -COR_{24}, -OR_{25}, -$CONR_{24}R_{25}$, -$CON(OR_{22})R_{23}$, -CO_2R_{26}, -C=$N(OR_{22})R_{23}$, and -$S(O)_mR_{23}$; wherein said C_1-C_{10} alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 hydrocarbylene), (C_3-C_8 cycloalkyl), (C_3-C_8 cycloalkylene), and (C_4-C_8 heterocycloalkyl) groups can be optionally

substituted with from one to three substituents independently selected form C_1-C_4 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 hydrocarbylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), C_1-C_4 haloalkyl, hydroxy, C_1-C_6 alkoxy, nitro, halo, cyano, -$NR_{24}R_{25}$, -$NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, -COR_{24}, -OR_{25}, -$CONR_{24}R_{25}$, CO_2R_{26}, -$CO(NOR_{22})R_{25}$, and -$S(O)_mR_{23}$; and wherein two adjacent substituents of the R_5 group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to R_5, which ring optionally can contain one, two, or three heterologous members independently selected from O, $S(O)_m$, and N, but not any -S-S-, -O-O-, -S-O-, or -N-S- bonds, and which ring is optionally substituted with C_1-C_4 alkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cyloalkylene)(C_3-C_8 cycloalkyl), C_1-C_4 haloalkyl, nitro, halo, cyano -$NR_{24}R_{25}$, $NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, -COR_{24}, -OR_{25}, -$CONR_{24}R_{25}$, CO_2R_{26}, -$CO(NOR_{26})R_{25}$, or -$S(O)_mR_{23}$; wherein one of said one to four optional substituents R_{27}, can further be selected from -$SO_2NH(C_1$-C_4 alkyl), -$SO_2NH(C_1$-C_4 alkylene)(C_3-C_8 cycloalkyl), $SO_2NH(C_3$-C_8 cycloalkyl), -$SO_2NH(C_3$-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -$SO_2N(C_1$-C_4 alkyl)(C_1-C_2 alkyl), -SO_2NH_2, -$NHSO_2(C_1$-C_4 alkyl), -$NHSO_2(C_3$-C_8 cycloalkyl), -$NHSO_2(C_1$-C_4 alkylene)(C_3-C_8 cycloalkyl), and -$NHSO_2(C_3$-C_8 cycloalkylene)(C_3-C_8 cycloalkyl); and wherein the hydrocarbyl, and hydrocarbylene groups of R_5 may independently optionally contain one double or triple bond;

R_6 is hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, -(C_1-C_6 alkylene)(C_3-C_8 cycloalkyl), or -(C_3 - C_8 cycloalkylene)(C_3-C_8 cycloalkyl), wherein said alkyl and cycloalkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

or R_6 and R_4 can together form an oxo (=O) group, or can be connected to form a 3-8 membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing one, two, or three heterologous ring members selected from O, SO_m, N, and NR_{12}, but not containing any -O-O-, -S-O-, -S-S-, or -N-S- bonds, and further optionally substituted with C_1- C_4 hydrocarbyl or C_3-C_6 cycloalkyl, wherein said C_1-C_4 hydrocarbyl substituent may optionally contain one double or triple bond;

R_{11} is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R_{12} is hydrogen or C_1-C_4 alkyl;

R_{22} is independently at each occurrence selected from hydrogen, C_1-C_{14} alkyl, C_1-C_{14} haloalkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_8 cycloalkyl, (C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), and (C_1-C_4) alkylene)(C_3-C_8 cycloalkyl);

R_{23} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_2-C_8 alkoxyalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, -(C_1-C_4 alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

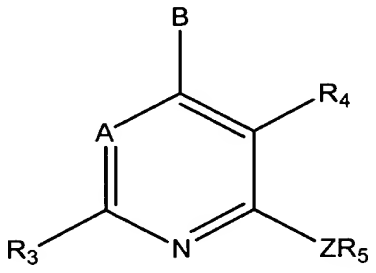
R_{24} and R_{25} are independently at each occurrence selected from hydrogen, -C_1-C_4 alkyl, C_1-C_4 haloalkyl, -(C_1-C_4 alkylene)OH, -(C_1-C_4 alkylene)-O-(C_1-C_4 alkyl), -(C_1-C_4 alkylene)-O-(C_3-C_5 cycloalkyl), C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -C_4-C_8 heterocyclohydrocarbyl , -(C_1-C_4 alkylene)(C_4-C_8 heterocyclohydrocarbyll), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocyclohydrocarbyl), aryl, and -(C_1-C_4 alkylene)(aryl), wherein the -C_4-C_8 heterocyclohydrocarbyl groups can each independently optionally be substituted with aryl, CH_2-aryl, or C_1-C_4 alkyl, and can optionally contain one or two double or triple bonds; or, when R_{24} and R_{25} are as $NR_{24}R_{25}$, -$C(O)NR_{24}R_{25}$, -(C_1.C_4 alkylene)$NR_{24}R_{25}$, or -$NHCONR_{24}R_{25}$, then $NR_{24}R_{25}$ may further optionally form a 4 to 8 membered heterocyclic ring optionally containing one or two further hetero members independently selected from $S(O)_m$, oxygen, nitrogen, and NR_{12}, and optionally containing from one to three double bonds;

R_{26} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, and -(C_1-C_4 alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that heterocyclohydrocarbylene groups of the compound of formula I, do not comprise any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and do not comprise more than two oxygen or $S(O)_m$ heterologous members.

Claim 2 (Twice Amended). A compound according to claim 1 of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is N;

B is -NR_1R_2, -$CR_1R_2R_{11}$, -$C(=CR_2R_{12})R_1$, -$NHCHR_1R_2$, -$OCHR_1R_2$, -$SCHR_1R_2$, -CHR_2OR_{12}, -CHR_2SR_{12}, -$C(S)R_2$ or -$C(O)R_2$;

Z is -NH, O, S, $N(C_1$-C_2 alkyl) or $C(R_{13}R_{14})$ wherein R_{13} and R_{14} are each independently, hydrogen, trifluoromethyl or methyl or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl;

R_1 is C_1-C_6 hydrocarbyl which may optionally be substituted with one or two substituents R_8 independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, CF_3, C_1.C_4 alkoxy, -O-CO-(C_1-C_4 hydrocarbyl), -O-CO-NH(C_1-C_4 hydrocarbyl), -O-CO-N(C_1-C_4 hydrocarbyl)(C_1-C_2 hydrocarbyl), -NH(C_1-C_4 hydrocarbyl), -N(C_1-C_2 alkyl)(C_1-C_4 hydrocarbyl), -S(C_1-C_4 alkyl), -N(C_1-C_4)CO(C_1-C_4 hydrocarbyl), -NHCO(C_1-C_4 hydrocarbyl), -COO(C_1-C_4 hydrocarbyl)hydrocarbyl, -CONH(C_1-C_4 hydrocarbyl), -CON(C_1-C_4 hydrocarbyl)(C_1-C_2 alkyl), CN, NO_2, -SO(C_1-C_4 hydrocarbyl) and -SO_2(C_1-C_4 hydrocarbyl), and wherein said C_1-C_6 hydrocarbyl and the (C_1-C_4)hydrocarbyl moieties in the foregoing R_1 groups may optionally contain one carbon-carbon double or triple bond;

R_2 is C_1-C_{12} hydrocarbyl, aryl or -(C_1-C_4 hydrocarbylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or -(C_1-C_6 alkylene)cycloalkyl, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said -(C_1-C_6 alkylene)cycloalkyl having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by N-R_9 wherein R_9 is hydrogen or C_1-C_4 alkyl; and wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro and C_1-C_4 alkyl, or with one substitutent selected from bromo, iodo, C_1-C_6 alkoxy, -O-CO-(C_1-C_6 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -S(C_1-C_6 alkyl), CN, NO_2, -SO(C_1-C_4 alkyl), and -SO_2(C_1-C_4 alkyl), and wherein said C_1-C_{12} hydrocarbyland the C_1-C_4 hydrocarboylene moiety of said -(C_1-C_4 hydrocarbylene)aryl may optionally contain one carbon-carbon double or triple bond;

or -NR_1R_2 or -$CR_1R_2R_{11}$ may form a saturated 5- to 8-membered carbocyclic ring which may optionally contain one or two carbon-carbon double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen or sulfur atom;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3, methylthio, methylsulfonyl, CH_2OH, or CH_2OCH_3;

R_4 is hydrogen, C_1-C_4 hydrocarbyl, fluoro, chloro, bromo, iodo, C_1-C_4 alkoxy, trifluoromethoxy, -CH_2OCH_3, -$CH_2OCH_2CH_3$, -$CH_2CH_2OCH_3$, -CH_2OF_3, CF_3, amino, nitro, -NH(C_1-C_4 alkyl), -N(CH_3)$_2$, -$NHCOCH_3$, -$NHCONHCH_3$, -SO_n(C_1-C_4 hydrocarbyl) wherein n is 0, 1 or 2, cyano, hydroxy, -CO(C_1-C_4 hydrocarbyl), -CHO, cyano or -COO(C_1-C_4 alkyl) wherein said C_1-C_4 hydrocarbyl may optionally contain one double or triple bond and may optionally be substituted with one substitutent selected from hydroxy, amino, -$NHCOCH_3$, -NH(C_1-C_2 alkyl), -N(C_1-C_2 alkyl)$_2$, -COO(C_1-C_4 alkyl), -CO(C_1-,C_4 alkyl), C_1-C_3 alkoxy, C_1-C_3 thioalkyl, fluoro, chloro, cyano and nitro;

R_5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each of the above groups R_5 is substituted with from one to three substituents independently selected from fluoro, chloro, C_1-C_6 alkyl, and C_1-C_6 alkoxy, or with one substitutent selected from hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, -(C_1-C_6 alkyl)O(C_1-C_6)alkyl, -$NHCH_3$, -$N(CH_3)_2$, -COOH, -COO(C_1-C_4 alkyl), -CO(C_1-C_4 alkyl), -SO_2NH(C_1-C_4 alkyl), -SO_2N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -SO_2NH_2, -$NHSO_2$(C_1-C_4 alkyl), -S(C_1-C_6 alkyl) and [-$_{SO2}$(C_1-C_6 alkyl)] <u>-SO_2(C_1-C_6 alkyl)</u>, and wherein the C_1-C_4 alkyl and C_1-C_6 alkyl moieties of the foregoing R_5 groups may optionally be substituted with one or two fluoro groups or with one substitutent selected from hydroxy, amino, methylamino, dimethylamino and acetyl;

R_{11} is hydrogen, hydroxy, fluoro, or methoxy;

R_{12} is hydrogen or C_1-C_4 alkyl; and

or a pharmaceutically acceptable salt of such compound.

Claim 13 (Amended). A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF or (b) a disorder or condition selected from inflammatory disorders, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception [such as fibromyalgia]; mood disorders, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases, gastrointestinal diseases; eating disorder; hemorrhagic stress; chemical dependencies or addictions; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage[,]; <u>excitotoxic neuronal damage;</u> [including cerebral ischemia;] epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

Claim 14 (Twice Amended). A pharmaceutical composition according to claim 13 for

the treatment of a disorder selected from inflammatory disorders; pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception; mood disorders [such as depression,, and postpartum depression]; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; human immunodeficiency virus (HIV) infections; neurodegenerative diseases; gastrointestinal diseases; eating disorders; chemical dependencies and addictions; obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; and hypoglycemia in a mammal[, including a human].

Claim 29 (Amended). A compound as claimed in claim 1 wherein [R24 and R25] R_{24} and R_{25} are selected from-CF_3, -CHF_2, CF_2CF_3, and CH_2CF_3[,].

Claim 32 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of depression, selected from the group consisting of major depression, single episode depression, recurrent depression, and child abuse induced depression.

Claim 36 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of [stress induced] immune dysfunctions induced by stress selected from the group consisting of [including] porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs.

Claim 39 (Amended). A pharmaceutical composition as claimed in claim [14] 44 for treatment of cerebral ischemia, selected from the group consisting of cerebral hippocampal ischemia[; excitotoxic neuronal damage].

Claim 40 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of social phobia, agoraphobia, or specific phobias.